REMARKS

Claims 1-15 were examined, claims 16-24 having been withdrawn from consideration. Claim 1 has been amended to add a limitation copied from claim 9, and claim 9 has been canceled accordingly. The amendment adds no new matter. Entry of the amendment and reconsideration of the claims in view of the following remarks are respectfully requested.

Claim Rejections under 35 U.S.C. § 102

Claims 1-3 and 6-15 were rejected based on Gao, *J. Bone Mineral Res.*, vol. 16(4), 605-614 (2001). According to the Examiner, Gao et al. "teach a parathyroid hormone (PTH) hormone control. The assay comprises a whole PTH component having amino acid 1-84 of PTH, and a PTH fragment having amino acid 7-84 of PTH which falls within the recited range, i.e. spanning position 2 through 33 of PTH of its N-terminal, and C-terminal spanning from 35 through position 84 of PTH, where Gao et al. teach storing the PTH in lyophilized form, e.g. protein matrix base (See page 606, right column, Materials and Methods-Chemical Reagents.)

Claims 2 was rejected because Gao allegedly also teaches "comparing the binding assay of IRMA and conventional Nichols assay by mixing the whole PTH component with the PTH fragment in a predetermined ratio (See Figure 2).

Claim 3 was also rejected because Gao allegedly teaches using synthetic method to generate the PTH components.

The applicant traverses this rejection. To establish a rejection for anticipation the Examiner must show that a reference discloses every limitation of the claim. Claim 1 requires an assay control comprising a known concentration of PTH components, with a "whole PTH component" and "a PTH fragment component", each having a defined structure; and "a protein matrix base." The 'and' indicates that both components must be present, along with a protein matrix base. The Examiner alleges the claim is anticipated by a disclosure of an assay, and the disclosure that some standards were lyophilized. However, the section that was cited for mentioning lyophilization says this:

> Standards and controls for the whole PTH IRMA were prepared by adding synthetic PTH(1-84) to a normal human serum that did not show any detectable PTH level with the intact PTH assay. The concentrations of the standard set were 0, 10, 16, 46, 165, 700, and 2300 pg/ml. All standards and controls were aliquoted, lyophilized, and stored at 2-8 °C.

This paragraph expressly describes the preparation of certain standards and controls, but the ONLY PTH component that it indicates was present in a lyophilized sample is PTH(1-84). It does not disclose a lyophilized assay control with a known concentration of a PTH fragment within the scope of the claims. The Examiner alleges that the assay in Gao contains a PTH fragment; but the claim is only anticipated by disclosure of a lyophilized assay control that has a PTH fragment in addition to a whole PTH, both at known concentrations. No assay control having both components was identified by the Examiner, let alone one having known concentrations of both together lyophilized with a protein matrix. Accordingly, claim 1 is not anticipated by the references.

Claims 2-3 depend from claim 1, and further limit it. Claims 2-3 are narrower than claim 1, and cannot be anticipated by the reference unless it is shown to teach all limitations of the independent claim. The additional disclosure of the reference that the Examiner pointed to as allegedly relevant to claim 2 is a graph that shows one line of data regarding PTH 7-84, and one for PTH 1-84; it does not disclose an 'assay control' or composition containing both together, and it does not disclose any composition that has been lyophilized with a protein matrix. The additional disclosure alleged to anticipate claim 3 does not cure the deficiencies with respect to claim 1, either. Accordingly, these claims are not anticipated by Gao.

Similarly, claims 6-15 depend directly or indirectly from claim 1. They are not anticipated by Gao for at least the same reasons that claim 1 is not anticipated. Accordingly, the anticipation rejections should be withdrawn.

Claim Rejections under 35 U.S.C. § 103

Claims 1-6 and 11-15 were rejected as obvious over Bouillon, et al. (*Clin. Chem.*, vol. 36, 271 (1990), in view of Holthuis, et al. (U.S. Patnet No. 5,496,801). According to the Examiner:

> Bouillon teaches a PTH assay control that "comprises a whole PTH component having amino acid 1-84 of PTH, and a PTH fragment having amino acid 23-84 of PTH which falls within the recited range... (See page 271, right column, Materials and Methods-Reagents). However, Bouillon et al. do not explicitly teach using protein matrix base to prolong the storage of the PTH peptides.
>
> Wang et al. [sic: this is presumed to mean 'Holthuis', the other reference that was cited by the Examiner] teach inactivated human serum albumin as protein matrix base to increase storage life of PTH (Col. 1, line 35-55).

The Examiner alleges that it would have been obvious, based on this, "to have provided Bouillon et al. with the lyophilizer as taught by Holthuis et al. in order to increase the storage live of the PTH peptides for subsequent analysis."

The applicant traverses this rejection. The cited passage in Holthuis, contrary to the Examiner's statement, does not teach or suggest that serum albumin prolongs the storage life of PTH peptides in a lyophilized state. Holthuis does relate to PTH formulations said to provide prolonged life, but those formulations do not require the presence of a protein matrix (e.g., in col. 2, the summary of the invention, Holthuis discloses one such mixture having PTH, mannitol and a citrate material).

The passage the Examiner cited from Holthuis is in the Background section of its specification, and it describes a number of previously reported formulations for PTH peptides. None of them appear to disclose or suggest the composition of claim 1. One of the formulations does include heat inactivated serum albumin, as the Examiner noted. However, that particular sentence says this: "Formulations representative of those employed for human studies include a human PTH(1-34) preparation consisting, upon reconstitution, of mannitol, heat inactivated human serum albumin, and caproic acid (a protease inhibitor) as absorption enhancer (see Reeve et al, 1976, *Calcif. Tissue Res.*, 21, Suppl., 469-77);..." It does NOT indicate that the albumin was used in a lyophilized composition, only that it was present in the reconstituted preparation (i.e., a non-lyophilized material), and it does NOT indicate that this particular formulation prolongs storage life of the peptide. Therefore, there would have been no motivation to select this particular formulation out of the many different ones disclosed by Holthuis for making a lyophilized assay control.

In addition, Bouillon does not disclose an assay control comprising known concentrations of whole PTH and a PTH fragment. The cited passage of the Materials and Methods section separately discloses the sources of a number of materials, including certain PTH peptides. It does not disclose or suggest a composition comprising whole PTH and a PTH fragment, and it does not disclose the combination of known concentrations of those materials in an assay control. The only PTH-type assay standards that the applicant sees in Bouillon are mentioned in the right hand column of page 272, where a PTH(53-84) standard and a PTH (1-84) standard are used. The PTH(53-84) standard is not within the range of PTH fragments in claim 1. The reference appears to use other PTH species as immunogens and to mention other PTH fragments in connection with antibodies used in the assays. Those uses of PTH fragments do not disclose or suggest the assay control of the present claims.

A *prima facie* case of obviousness requires the Office to show that the cited references disclose or suggest all of the limitations of the claim, and that a person of ordinary skill would have been motivated to combine or modify the references to arrive at the claimed invention and a reasonable expectation of success when making the combination or modification. Here, there is no motivation to combine the two references: the asserted motivation is not supported by the reference. Moreover, neither of the cited references discloses or suggests the assay control of claim 1, comprising a PTH fragment and whole PTH in known concentrations. Accordingly, no *prima facie* case for an obviousness rejection of claim 1 has been established. This rejection should be withdrawn.

For at least these reasons, the obviousness rejections of claims 2-6 and 11-15 based on this combination of references should also be withdrawn.

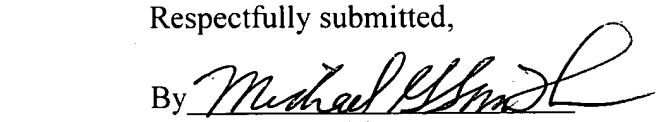
In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is

determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 532212001900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 13, 2006

Respectfully submitted,

By 

Michael G. Smith
Registration No.: 44,422
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 720-5113